Mutations in CBL occur frequently in juvenile myelomonocytic leukemia.

Journal: Blood

Publication Year: 2009

Authors: Mignon L Loh, Debbie S Sakai, Christian Flotho, Michelle Kang, Manfred Fliegauf, Sophie Archambeault, Charles G Mullighan, Leslie Chen, Eva Bergstraesser, Carlos E Bueso-Ramos, Peter D Emanuel, Henrik Hasle, Jean-Pierre Issa, Marry M van den Heuvel-Eibrink, Franco Locatelli, Jan Stary, Monica Trebo, Marcin Wlodarski, Marco Zecca, Kevin M Shannon, Charlotte M Niemeyer

PubMed link: 19571318

Funding Grants: Training Grant I

Public Summary:

Scientific Abstract:
Juvenile myelomonocytic leukemia is an aggressive myeloproliferative disorder characterized by malignant transformation in the hematopoietic stem cell compartment with proliferation of differentiated progeny. Seventy-five percent of patients harbor mutations in the NF1, NRAS, KRAS, or PTPN11 genes, which encode components of Ras signaling networks. Using single nucleotide polymorphism arrays, we identified a region of 11q isodisomy that contains the CBL gene in several JMML samples, and subsequently identified CBL mutations in 27 of 159 JMML samples. Thirteen of these mutations alter codon Y371. In this report, we also demonstrate that CBL and RAS/PTPN11 mutations were mutually exclusive in these patients. Moreover, the exclusivity of CBL mutations with respect to other Ras pathway-associated mutations indicates that CBL may have a role in deregulating this key pathway in JMML.